## CANCER RESEARCH UNIT VETERANS ADMINISTRATION MEDICAL CENTER

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Dr. Harold E. Varmus Chairman, Retrovirus Study Group Department of Microbiology and Immunology University of California San Francisco, Calif. 94143

Dear Harold,

Thank you for your letter of April 26th requesting my opinion about a suitable species name for the causative agent of the acquired immune deficiency syndrome (AIDS).

You have received recently from Dr. Gallo a letter (dated April 8th), emphasizing the reasons which in his and his group's opinion, would support the term HTLV-III for the AIDS virus discovered in his laboratory. I received from Bob a copy of that letter. I assume that you have also received a copy of my letter to Dr. M. Essex, replying to his request for my comments on the discussed designation of the AIDS virus.

The Lymphadenopathy-Associated Virus (LAV), independently discovered by L. Montagnier and his group at the Pasteur Institute in Paris, is very closely related to, and probably identical with, the HTLV-III virus. I am sure that you and other members of your group are thoroughly familiar with this problem, which further complicates the question of the designation of the AIDS virus.

The term HTLV-III (LAV) could be used in situations such as may arise when discussing the differential diagnosis in front of the patient or his or her family members, since the disease itself has a very high mortality and is being greatly feared. It also would be consistent with a designation to which all concerned physicians and health personnel are used to. However, as an additional designation, the term "AIDS virus" could be used also, or, perhaps, as the principal name.

It is true that the AIDS virus was discovered by Gallo and his coworkers in studies which were a continuation of his initial studies on human T-cell leukemia virus (HTLV-I).

However, although HTLV-III has certain common features with HTLV-I, it is essentially a different virus; it has a different morphology on electron microscopic examination, its genome has a different nucleotide sequence, and, most important of all, it causes a different disease syndrome.

We had a relatively similar situation when the first mammalian leukemogenic virus was discovered in 1951 in experiments carried out on mice. I designated this virus after its discovery in my laboratory "the mouse leukemia virus". Others later called it "the murine leukemia virus". This virus causes a variety of forms of leukemia and lymphomas following inoculation into newborn mice; it is also naturally transmitted in that species. In the course of our experiments in which we inoculated newborn mice with the mouse leukemia virus, we observed that a few mice, instead of leukemia, developed multicentric salivary gland tumors, particularly those of the parotid glands. In addition, some of these mice developed also mammary carcinomas, subcutaneous sarcomas, adrenal gland tumors and other neoplasms. Some investigators theorized that the same mouse leukemia virus may be able to induce either leukemia, or solid tumors, such as sarcomas or carcinomas. The problem was solved before very long when we determined that filtered extracts prepared from leukemic mouse organs contain not only the mouse leukemia virus, but also another distinct virus, smaller and more resistant to heat. It soon became clear that this smaller tumor virus is responsible for the induction of salivary gland carcinomas and other solid tumors; this virus was designated at first "parotid gland tumor virus" and later renamed by B. Eddy and S. Stewart as "polyoma virus"; it was soon realized that this newly discovered virus is of a different nature than the mouse leukemia virus, even though it was discovered in the course of our initial experiments inspired by our determination to demonstrate viral etiology of mouse leukemia.

Thus, the fact that the AIDS virus was discovered by Dr. Gallo and his group apparently as a follow-up of his initial studies on HTLV-I, may not necessarily imply that it should bear a similar designation. HTLV-III is a different virus, even though it shares certain basic features with HTLV-I.

Among the basic common disease syndromes induced with both, the HTLV-I and the AIDS viruses, is a breakdown of immunity in the infected hosts. However, the AIDS virus tends to cause a practically complete paralysis of the host's resistance, incomparably more pronounced, than that caused by HTLV-I in man, or by other leukemogenic viruses in other animal species, such as cats, cattle, mice or rats. Furthermore, like other leukemogenic viruses, HTLV-I may induce proliferation of cells of the hematopoietic system

resulting in the development of leukemia and/or lymphomas; whereas the AIDS virus causes essentially a breakdown of immunity by destroying certain T lymphocytes, and is only indirectly oncogenic, since breakdown in host resistance may result in rapid proliferation and spread not only of opportunistic bacterial and other parasitic infections, but also that of certain neoplastic diseases, such as Kaposi sarcoma.

Should the AIDS virus bear the prefix "human"? Not necessarily so. As an example, human adenoviruses are usually plainly called adenoviruses, without the prefix "human", even though there exist similar adenoviruses adapted to, and prevalent in, different animal species. The same is true for other viruses causing disease in humans, which have related virus strains pathogenic for other animal species, such as herpesviruses, or those of the polyoma group.

In conclusion, I would rather refrain from giving a straight forward suggestion for AIDS virus designation, but prefer to give you some thoughts on this problem as they have come to my mind. We also have to accept the fact that all three terms, HTLV-III, LAV, and AIDS virus, are now generally used by virologists, clinicians, and hospital workers, as well as by laymen, and it may not be easy to either eliminate, or exclusively substitute, either of these terms.

With July regular

Sincerely yours,

Ludwik Gross, M.D.

Chief, Cancer Research Unit